UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/334,969	06/17/99	JAKOBSEN B	102286.410

HM22/0117

HOLLIE L BAKER
HALE AND DORR LLP
60 STATE STREET
BOSTON MA 02109

EXAMINER	
DIBRINO, M	
ART UNIT	**PAPER NUMBER**
1644	12

DATE MAILED: 01/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/334,969	Karsten et al
Examiner	**Group Art Unit**
Marianne DiBrino	1644

☒ Responsive to communication(s) filed on Nov 5, 1999, 6/17/99 & 10/30/00

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-30 and 32 is/are pending in the applicat

Of the above, claim(s) 28-30 and 32 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-27 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9, filed 1/21/00 & 11/5/99, respectively

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's amendments filed 11/5/99 (Paper No. 7) and 6/17/99 (Papers No. 4 and 5) are acknowledged and have been entered.

Claims 1-30 and 32 are pending.

2. Applicant's election without traverse of Group I (claims 1-27), and species of the specific complex of a TCR tetramer comprising four αβ dimers and the specific linker molecule of avidin in Paper No. 7 is acknowledged.

Claims 1-27 read on the elected species and are presently being examined.

Accordingly, claims 28-30 and 32 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

3. The abstract of the disclosure is objected to because: the abstract should appear as one paragraph. Correction is required. See MPEP § 608.01(b).

4. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(I) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.

(l) Sequence Listing (see 37 CFR 1.821-1.825).

5. The disclosure is objected to because of the following informalities:

The use of the trademarks "SUPERDEX", "POROS", "BIACORE", "PHARMACIA FPLC", "BIOCAD", "TRITON-X", "DYNABEADS", "PBLUESCRIPT", "XL-BLUE", "BIG DYE", "BIOCAD", "SEMIPHOR", "MINIGEL" and "CELLQUEST" have been noted in this application. It should be capitalized or accompanied by the ™ or ® symbol wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Each letter of the trademark must be capitalized. See MPEP 608.1(V) and Appendix 1.

Appropriate corrections are required.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 7-16, 22 and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Regarding claims 7 and 8, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

b. Claim 24 is indefinite in the recitation of "attached to a particle" because it is not clear what is meant by the term "particle".

c. The term "multimerised" recited in claims 10 and 11, the terms "dimerisation", "heterodimerised" and "heterodimerisation" in claims 12, 14, 15 and 16, the term "disulphide"and the term "derivatised" in claim 22 should be changed to "multimerized", "dimerization", "heterodimerized", "heterodimerization", "disulfide" and "derivatized", respectively.

d. Claim 12 is indefinite in the recitation of the phrase "a first heterologous C-terminal dimerisation peptide" because it is unclear what the said peptide is heterologous to.

8. Claims 14 and 15 are objected to under 37 CFR § 1.75© as being in improper form because a multiple dependent claim can not depend from any other multiple dependent claim.

9. The Chang et al reference and the Golden et al reference crossed out in the Form 1449 filed 1/21/00 has been considered and initialed on the Form 1449 filed 11/5/99, as the said references were cited in duplicate. The 5,328,485 reference on the Form 1449 filed 1/21/00 has not been considered because it is an incorrect citation.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-9, 10, 11, 17, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/35991 (Applicant's IDS reference in the Form 1449 filed 1/21/00).

WO 97/35991 teaches soluble recombinant divalent and multivalent analogs (including tetravalent, i.e., a tetramer) of heterodimeric proteins and pharmaceutical compositions thereof, including αβ TCR that possess enhanced affinity for their target molecules, said αβ TCR chains further comprising Ig linker molecules (i.e., dimerisation peptides) and which may further comprise a toxin, and/or may be further linked by association via avidin (especially page 8, line 31, page 9, lines 1-4, page 10, lines 27-31, page 11, lines 1-7, page 14, lines 7-16, Figure 1D and legend, claims 1-5, 8, 10-14, 17, 27 and 28, page 1, lines 14-17, page 16, lines 1-14). With regard to instant claim 17, the recitation of a method wherein the claimed product is made carries no patentable weight in these product claims. Claims 8 and 9 are included in the instant rejection because WO 97/35991 inherently teaches the limitations of the said claims because the multimers of WO 97/35991 are linked by avidin which is the binding partner for biotin.

The reference teachings anticipate the claimed invention.

12. Claims 1-4 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Paliwal et al (J. Immunol., Vol. 159: 1718-1727, 1997, Applicant's IDS reference in the Form 1449 filed 1/21/00).

Paliwal et al teach recombinant pentameric soluble αβ TCR (sTCR) (especially Abstract and page 1726, column 1, 2nd paragraph). With regard to instant claim 17, the recitation of a method wherein the claimed product is made carries no patentable weight in these product claims.

The reference teachings anticipate the claimed invention.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-9, 10-12, 14-18, 26 and 27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 97/35991 (Applicant's IDS reference in the Form 1449 filed 1/31/00) in view of Golden et al (J. Immunol. Meth., Vol. 206: 163-169, 1997, Applicant's IDS reference in the Form 1449 filed 11/5/99), O'Shea et al (Science, Vol. 245: 646-648, 1989, Applicant's IDS reference in the Form 1449 filed 11/5/99).

WO 97/35991 teaches soluble (i.e., extracellular domains) recombinant divalent and multivalent analogs (including tetravalent, i.e., a tetramer) of heterodimeric proteins and pharmaceutical compositions thereof, including αβ TCR that possess enhanced affinity for their target molecules, said αβ TCRs being associated via Ig linker molecules which may further comprise a toxin, and/or may be further linked by association via avidin (especially page 8, line 31, page 9, lines 1-4, page 10, lines 27-31, page 11, lines 1-7, page 14, lines 7-16, Figure 1D and legend, claims 1-5, 8, 10-14, 17, 27 and 28, page 1, lines 14-17, page 16, lines 1-14). With regard to instant claim 17, the recitation of a method wherein the claimed product is made carries no patentable weight in these product claims. In addition, WO 97/35991 teaches that the multimeric soluble TCR complexes may be useful in defining the specific peptide/MHC ligands recognized by uncharacterized tumor-specific T cells and T cells involved in autoimmune responses (especially page 10, lines 27-31 and page 11, line 1). WO 97/35991 also teaches production of the multimers in baculovirus with a yield of about 1 ug/ml (i.e., about 1 mg/L). WO 97/35991 also teaches short flexible Gly-Ser spacers between the TCR chain and the Ig portion (Figure 1D and legend).

WO 97/35991 does not teach multivalent soluble αβ TCR wherein each chain has a heterologous C-terminal dimerisation peptide which is a coiled coil domain (such as a leucine zipper from c-fos and c-jun) dimerization peptide, which dimerize, one with the other, and wherein a short flexible linker is between the TCR and the dimerisation domain, and further, wherein a disulfide bond present in the native TCR between the α and β chains adjacent to the cytoplasmic domain is absent from the recombinant TCR.

Golden et al teach soluble heterodimeric TCR comprising an α and a β chain, each chain comprising a leucine zipper which dimerizes, one with the other, produced in E. coli at yields of 4-5 mg/L (especially Abstract).

O'Shea et al teach heterodimer formation through leucine zippers from c-fos and c-jun (especially Abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have substituted the soluble heterodimeric TCR of Golden et al, with the Gly-Ser linker of WO 97/35991, as the monomeric TCR in the multimers of WO 97/35991 that were mulitmerized by avidin and to have produced the proteins in E. coli as taught by Golden et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made used any leucine zipper of appropriate stability such as the leucine zippers from c-fos and c-jun taught by O'Shea et al in the soluble heterodimeric TCR of Golden et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to increase the yield of correctly folded soluble TCR as taught by Golden et al.

With regard to instant claims 9 and 18, one of ordinary skill in the art at the time the invention was made would have been aware that biotin is the binding partner for avidin, and that biotin would have been incorporated into the monomer TCR in order that the monomer TCR could have been linked via avidin to form multimers. With regard to instant claim 18, one of ordinary skill in the art at the time the invention was made would have been aware that the C-terminus of the heterodimer chain would be the optimal location for biotinylation, rather than at the N-terminus where preservation of antigen binding function was paramount.

15. Claim 13 is rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 97/35991 in view of Golden et al (J. Immunol. Meth., Vol. 206: 163-169, 1997, Applicant's IDS reference in the Form 1449 filed 11/5/99) as applied to claims 1-9, 10-12, 14-18, 26 and 27 above, and further in view of Garboczi et al (J. Immunology, Volume 157: 5403-5410, 1996, Applicant's IDS reference in the Form 1449 filed 11/5/99).

WO 97/35991 and Golden et al have been discussed supra.

WO 97/35991 and Golden et al do not teach the TCR complex of instant claim 13, wherein the disulfide bond between the α and β chain of the TCR are absent.

Garbozci et al teach a soluble TCR without the interchain disulfide bond present in native TCRs, and that the heterodimerization, refolding and antigenic specificity of the TCR do not require its interchain disulfide bond, transmembrane segments or glycosylation (especially Abstract and page 5408, column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have to have a recombinant TCR as taught by the combination of WO 97/35991 and Golden et al without the disulfide bond, as taught by Garboczi et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because Garboczi et al teach that the presence of said bond is not important for heterodimerization and refolding, and further in order to facilitate the production of soluble correctly associated TCR, i.e., in order to insure that disulfide bonds did not form between homologous chains or with other contaminating proteins during purification.

16. Claims 1, 24 and 25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 97/35991 in view of U.S. Patent No. 5,635,363 (Applicant's IDS reference in Form 1449 filed 11/5/99).

WO 97/35991 has been discussed supra. In addition, WO 97/35991 teaches that the multimeric soluble TCR complexes may be useful in defining the specific peptide/MHC ligands recognized by uncharacterized tumor-specific T cells and T cells involved in autoimmune responses (especially page 10, lines 27-31 and page 11, line 1).

WO 97/35991 does not teach a mutimeric TCR complex comprising a detectable label, nor attached to a "particle".

U.S. Patent No. 5,635,363 dicloses soluble MHC/peptide tetramers which are biotinylated and multimerized with streptavidin or with avidin and which further comprise a light detectable label FITC or an enzyme (especially claims) and which further may be bound to an insoluble support such as a bead, i.e., a "particle", for the purpose of assay (especially column 8, lines 4-16).

It would have been prima facie obvious to one of ordinary skill at the time the invention was made to have biotinylated, as disclosed by the '363 patent for soluble MHC/peptide tetramers, the soluble TCR complexes of WO 97/35991 and to have multimerized them using avidin, and further to have labeled them with a detectable label such as is disclosed by the '363 patent for the MHC/peptide tetramers, or to have bound them to a bead.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to form more avid multimers because WO 97/35991 teaches multimers and tetramers and both WO 97/35991 and the '363 patent teach use of avidin for multimerization of heterodimeric proteins, and also because one of ordinary skill in the art at the time the invention was made would have been motivated to facilitate detection because WO 97/35991 teaches that multimeric soluble TCR complexes may be useful in defining the specific peptide/MHC ligands recognized by uncharacterized tumor-specific T cells and T cells involved in autoimmune responses.

17. Claims 1 and 19-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 97/35991 in view of Ahmad et al (Cancer Res., Volume 53: 1484-1488, 1993).

WO 97/35991 has been discussed supra.

WO 97/35991 does not teach a multimeric TCR complex attached to a lipid vescicle via derivatised lipid components of the vesicle.

Ahmad et al teach attachment of a biotinylated targeting antibody attached to the surface of a liposome containing biotinylated phosphatidylethanolamine by means of an avidin linker (especially Introduction and Liposome Preparation on page 1484). Ahmad et al further teach that liposomes containing lipid derivatives of polyethylene glycol have circulation times sufficiently long to allow for effective in vivo drug delivery.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have attached the multimeric TCR complex of WO 97/35991 to the liposome of Ahmad et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to effectively deliver in vivo the multimeric TCR complex taught by WO 97/35991 to be useful for in vivo therapy. Claim 23 is included in this rejection because it would also have been prima facie obvious to embed the TCR complex in the liposome of Ahmad et al because Ahmad et al teach effective delivery of a substance embedded in the liposome rather than attached to the surface via a derivatized component of the liposome (especially Abstract). Instant claim 24 is included in this rejection because the claim limitation "particle" can read on "liposome" of the art reference.

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-12, 14-18, 26 and 27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-8, 10, 20 and 21 of copending Application No. 09/335,087 in view of the combination of WO 97/35991, Golden et al and O'Shea et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the multimers of the instant application are obvious variants of the TCR multimer of claim 21 of the '087 application and of the TCR monomers of claims 1, 2, 4-8, 10 and 20 because the combination of references provides the motivation for multimerization of TCR monomers having the structural or functional limitations of the instant claims. Also, in the '087 application the monomers of claims 1, 2, 4-8, 10 and 20 and the multimers of claim 21 were not held to be patentably distinct in the restriction requirement.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claim 13 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of copending Application No. 09/335,087 in view of the combination of WO 97/35991, Golden et al, O'Shea et al and Garboczi et al as discussed and set forth above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the multimers of instant claim 13 are obvious variants of the TCR monomer of claim 3 of the '087 application because the combination of references provides the motivation for multimerization of TCR monomers having the structural or functional limitations of the claimed monomers and because Garboczi et al provides the motivation for making a TCR monomer or multimer lacking a disulfide bond present in native TCRs between the heterodimer chains. Also, in the '087 application monomers and multimers were not held to be patentably distinct in the restriction requirement.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

21. Claims 24 and 25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of copending Application No. 09/335,087 in view of the combination of WO 97/35991 and U.S. Patent 5,635,363 as discussed and set forth above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the multimers of instant claims 24 and 25 are obvious variants of the TCR monomer of claim 9 of the '087 application because the combination of references provides the motivation for multimerization of TCR monomers having the structural or functional limitations of the claimed monomers and because U.S. Patent 5,635,363 provides the motivation for making a TCR multimer attached to a particle or

labeled with a detectable label. Also, in the '087 application monomers and multimers were not held to be patentably distinct in the restriction requirement.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

22. Claims 19-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 21 of copending Application No. 09/335,087 in view of the combination of WO 97/35991 and Ahmad et al as discussed and set forth above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the multimers of the instant application are obvious variants of the TCR multimer of the claim 21 of the '087 application because Ahmad et al provide the motivation for attaching the multimer to a lipid bilayer or liposome.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

23. Claims 1-27 are directed to an invention not patentably distinct from claims 1-10, 20 and 21 of commonly assigned 09/335,087. Specifically, the claims are not considered to be distinct for the reasons enumerated in the obviousness-type double patenting rejection above.

24. Commonly assigned 09/335,087, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g).

25. No claim is allowed.

26. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
January 13, 2000

Christina Chan
CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640